

Alovudine



Drug Description

Alovudine is a synthesized 3'fluoro-substituted derivative of 3'-deoxythymidine, a pyrimidine nucleoside analogue. Alovudine is structurally similar to AZT, differing only at the 2' and 3' positions of the ribose moiety. AZT is characterized by an azido group at the 3' position; alovudine has a fluoro group at this position. [1]

HIV/AIDS-Related Uses

Alovudine is a nucleoside reverse transcriptase inhibitor (NRTI) being investigated for the treatment of HIV. Alovudine is similar to zidovudine. Initial investigation of alovudine was stopped due to unacceptable levels of hematologic toxicity and no clear benefit over zidovudine.[2]

Pharmacology

Alovudine inhibits HIV replication by mimicking thymidine. When alovudine is incorporated into the DNA strand during synthesis, premature chain termination occurs.[3]

Absorption of alovudine is rapid; peak plasma concentration (Cmax) is reached within 90 minutes. Cmax is variable, with up to a three-fold difference in Cmax among patients at the same dose level. The area under the concentration-time curve (AUC) appears to be less variable, with coefficients of variation ranging from 14% to 21%. Increase in Cmax and AUC were proportional to the increment in dose; mean Cmax's were 234, 529, 1130, and 1662 ng/ml at the dose levels 0.13, 0.3, 0.67, or 1.3 mg/kg. AUC's were 612, 1110, 2493, and 5190 ng hr/ml for each group. The elimination half-life of alovudine ranged from 2.5 to 6.3 hours (mean 3.1 to 4.3 hours), independent of dose and three-fold longer than the half-life of AZT.[4] [5]

In a concentration-controlled trial involving 14 HIV infected patients, unacceptable hematologic toxicity occurred when the AUC curve during a 12-hour dosing interval (AUC12) was greater than or equal to 300 ng hr/ml. In this trial, alovudine resulted in a concentration-dependent reduction in p24 antigen and peripheral blood mononuclear cell (PBMC)

HIV titers within 4 weeks of treatment initiation.[6]

Alovudine has potent activity in vitro against multi-drug resistant HIV strains. Multidrug resistant isolates that exhibit 5-fold to 100-fold increased resistance to AZT show IC50 values for alovudine of 0.0014 to 0.0162 microM, which are lower than or similar to that of wild type virus. In this study, cellular toxicities of alovudine and AZT fell into a similar range in PBMCs and development of alovudine resistant isolates was slower than for other NRTIs.[7]

Adverse Events/Toxicity

Earlier studies of alovudine at doses of 20 mg/day showed unacceptable hematologic toxicity (severe anemia and neutropenia).[8]

Clinical Trials

For information on clinical trials that involve Alovudine, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: Alovudine AND HIV Infections.

Dosing Information

Mode of Delivery: Oral.[9]

Dosage Form: Liquid.[10]

Chemistry

CAS Name: Thymidine, 3'-deoxy-3'-fluoro-[11]

CAS Number: 25526-93-6[12]

Molecular formula: C10-H13-F-N2-04[13]

Molecular weight: 244.22[14]

Other Names

3'-Deoxy-3'-fluorothymidine[15]

3'-Fluoro-3'-deoxythymidine[16]

Alovudine



Other Names (cont.)

3'-Fluorodeoxythymidine[17]

3'-Fluorothymidine[18]

BRN 0754299[19]

FLT[20]

FddT[21]

NSC 140025[22]

MIV-310[23]

Further Reading

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Manufacturer Information

Alovudine
Boehringer Ingelheim GmbH
55216 Ingelheim am Rehin
Germany

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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